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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,226	03/06/2002	Dieter Naumann	2364-011622	5569
7590	12/31/2003			
Richard L Byrne 700 Koppers Building 436 Seventh Avenue Pittsburgh, PA 15219-1818			EXAMINER GAKH, YELENA G	
			ART UNIT 1743	PAPER NUMBER

DATE MAILED: 12/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/009,226	Applicant(s) NAUMANN ET AL.	
	Examiner Yelena G. Gakh, Ph.D.	Art Unit 1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 March 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-30 is/are rejected.
- 7) ☒ Claim(s) 11, 13, 14 and 28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 March 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>07/22/02</u> . | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

1. Preliminary Amendment filed on 03/06/02 is acknowledged. Claims 1-10 are cancelled. Claims 11-30 are pending in the application.

Drawings

2. The drawings are objected to because the word "Figure" is misspelled in all of them. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

3. The specification is objected to as containing language that is not always clear and definite.

In the Summary of the Invention, the sentence "it is thus *the problem* of this invention to provide a method for detecting TSE-induced pathologic changes in tissues" does not seem right, since the invention should either *solve* the problem, or has a *purpose* of providing the method. Correction is requested.

The expression "classifying infrared spectra" is not clear and is not explained in the specification. Classifying IR spectra according to which classification? There are no real "classes" of IR spectra; the classification appears to be related to differences in IR spectra for TSE-infected and non-infected tissues; however, it is not clearly expressed in the specification.

Claim Objections

4. Claim 11 is objected to because of the following informalities: it contains abbreviations (TSE, BSE), which should be accompanied by the full names; also, step (a) is not written in a

clear language, since it is not apparent, what the expression "*that* the spectral characteristics ... are recorded" refers to. The suggested correction: "and recording the spectral characteristics".

Claims 13 and 14 recite wrong wavenumbers: in claim 13 it should be "10000 cm⁻¹", while in claim 14 - "1000 cm⁻¹". Correction is required.

Double Patenting

5. Claim 28 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 14. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 11-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites "a method for diagnosing TSE-induced pathological changes", comprising the step of providing a tissue sample, which is already TSE-changed; this makes the purpose of the method unclear. If the sample is *apriori* TSE-changed, than why such diagnosis is required, and especially, how IR spectra of this sample can be classified as normal? If this is *any* tissue sample showing pathological changes, with no preliminary knowledge of the cause of the pathology, than the word "TSE" should be removed from the language of step (a).

Claim 21 is rejected as reciting the limitation "the human organs", which lacks antecedent basis, as no "human organs" is recited in the parent claim 11. The claim should presumably depend on claim 12, rather than 11.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. **Claims 11-15, 17-21, 24-30** are rejected under 35 U.S.C. 103(a) as being unpatentable over Caughey et al. (Biochemistry, 1991, IDS,) in view of Choo et al. (Biophys. J., 1996, IDS).

Caughey teaches a method of diagnosis of TSE (scrapie) disease by comparison of IR spectra of protein PrP extracted from normal and TSE-modified tissue, with the spectra reflecting changes in a secondary structure of protein PrP responsible for the disease. "The results of this study suggest that the infrared techniques applied here to PrP-res 27-30 will allow the direct comparison of the conformations of the normal and scrapie-associated PrP forms and their variants once sufficient quantities of the purified PrP species become available. The enhanced resolution afforded by second-derivative analysis of infrared spectra provides individual

conformational "fingerprints" of proteins, e.g., multiple bands in both the turn and β -sheet regions, that can allow, more detailed comparison of conformation than is reflected in the overall secondary structure compositions" (page 678, right column). "For each spectrum, a 1000-scan interferogram was collected in the single-band mode with 2 cm^{-1} resolution and a 1 cm^{-1} interval from 4000 to 1000 cm^{-1} . Reference spectra were recorded under identical conditions with only the media in which protein was suspended in the cell" (page 7673, right column, Infrared Spectroscopy).

Caughey does not teach direct infrared irradiation of the tissue samples.

Choo-1996 discloses "in situ characterization of β -amyloid in Alzheimer's diseases tissue by synchrotron Fourier Transform Infrared microspectroscopy", comprising spectroscopic mapping of AD tissue, which indicates the presence of amyloid proteins with conformation characteristic of Alzheimer's diseases (pages 1675 and 1676) and comparing IR spectra of normal and Alzheimer's diseased grey and white matter (Figure 2).

It would have been obvious for anyone of ordinary skill in the art to modify Caughey's method of diagnosis of TSE (scrapie) disease by implying FTIR microspectroscopy, taught by Choo for AD diagnosis, because it allows to obtain IR spectra directly from tissue, which is less disruptive for the sample, and because it is more advanced regarding resolution and sensitivity.

12. **Claims 16, 22 and 23** are rejected under 35 U.S.C. 103(a) as being unpatentable over Caughey in view of Choo-1996, as applied to claims 11-13, 15, 17-21, 24-30 above, and further in view of Choo et al. (Biospectroscopy, 1995, Abstract).

While Caughey in view of Choo-1996 do not disclose multivariate analysis of IR spectra, Choo-1995 teaches multivariate analysis of IR spectra of human central nervous system tissue in diagnosing Alzheimer's disease, emphasizing that "classification of tissue as either control or AD was achieved with a success rate of 100%" by applying multivariate methods of analysis.

It would have been obvious for anyone of ordinary skill in the art to apply multivariate analysis of IR spectra in Caughey-Choo-1996's method, as taught by Choo-1995, because Choo-1995 indicates perfect success rate in classifying normal versus diseased tissues based on IR spectra, when analyzed by multivariate techniques.

Conclusion

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. *Krishnamurthy (US 6,399,314 B1)* teaches "methods of detection of amyloidogenic proteins" in diagnosis of neurodegenerative disease such as "subacute spongiform encephalopathy, such as but not limited to, scrapie, Creutzfeldt-Jakob disease, Gerstmann-Straussler disease, kuru, chronic wasting disease of mule-deer and elk, bovine spongiform encephalopathy of cattle, and mink transmissible encephalopathy" (col. 9, lines 43-47), using IR spectra. *Budinova et al. (Chemicke Listy)* discloses application of IR spectroscopy in the study of human tissues with a review of 61 references.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (703) 306-5906. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.



Yelena G. Gakh
12/13/03